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Color vision in epileptic adolescents treated with valproate and carbamazepine

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KEYWORDS
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SWAP

Summary *Objective*: The aims of our study were to evaluate whether deficits in color vision exist in epileptic adolescents, to study if monotherapy with valproic acid (VPA) and carbamazepine (CBZ) can affect color vision, and to determine the possible relationship between abnormal color vision tests and AEDs dosage and their serum concentrations. *Patients*: We examined 45 epileptic patients before the beginning of therapy and after 1 year of VPA or CBZ monotherapy and 40 sex- and age-matched healthy controls. *Methods*: Color vision was evaluated with Farnsworth Munsell 100 (FM100) hue test and achromatic and short-wavelength automated perimetry (SWAP). *Statistical analysis*: To evaluate intergroup differences we used ANOVA with Scheffe's post hoc test, when appropriate. Repeated measures ANOVA was used to evaluate the intragroup modifications of total error score (TES) and perimetric threshold during the follow-up. Pearson's correlation test was performed to correlate chromatic sense and perimetric data and AEDs dosage and serum concentrations. *Results*: Before the beginning of therapy, there were no differences in central color vision and SWAP between controls and epileptic patients. After 1 year, patients treated with VPA or CBZ showed a deficit in FM100 hue test and SWAP parameters while no significant deficit was found in achromatic perimetry. In particular, with the FM100 hue test a higher number of errors was found in both groups of patients (CBZ patients: 166.00 ± 27.72 TES; VPA patients: 151.19 ± 44.09, $P < 0.001$) in comparison with controls (controls: 109.29 ± 24.73) and baseline values (CBZ patients: 110.65 ± 22.9; VPA patients 107.43 ± 21.70). With SWAP patients of both groups showed significant variation of foveal threshold (controls: 21.07 ± 2.01 dB; CBZ patients: 19.35 ± 1.32, $P < 0.001$; VPA patients: 18.88 ± 1.89, $P < 0.001$), full-field mean threshold perimetric sensitivity (controls: 18.50 ± 1.24 dB; CBZ patients: 16.60 ± 1.47, $P < 0.001$; VPA patients: 16.23 ± 1.55, $P < 0.001$) and mean threshold perimetric sensitivity of the three evaluated subareas of the visual field (area 1 controls: 21.01 ± 1.15; CBZ patients: 19.45 ± 1.74, $P = 0.001$; VPA patients: 18.25 ± 1.61, $P < 0.001$; area 2 controls: 18.40 ± 1.43; CBZ patients: 16.07 ± 1.58, $P < 0.001$; VPA patients: 16.13 ± 1.46,

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$P = 0.001$; area 3 controls: 17.20 ± 1.49; CBZ patients: 14.28 ± 1.51, $P < 0.001$; VPA patients: 14.31 ± 2.90, $P = 0.001$). *Conclusions*: Our study demonstrates that treatment with VPA or CBZ can affect significantly both central and paracentral color vision after a short treatment period.
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Introduction

Previous studies have suggested that antiepileptic drugs (AEDs) may have an influence on visual functions.[1–7] In particular, carbamazepine (CBZ) and valproic acid (VPA) can produce a significant impairment of color perception.[8,9] Recent studies on visual function have indicated that epilepsy patients treated with CBZ or VPA have an accumulation of errors along the blue axis in the Farnsworth Munsell 100 (FM100) hue test.[3] Moreover, the color contrast tests differentiate visual system disorders even when visual impairment is still mild; therefore, color contrast evaluation may be more sensitive than conventional luminance tests.[10,11] In spite of several papers that have investigated visual perception tests in epileptic patients receiving AEDs, the data in the literature are conflicting; nevertheless there is no study carried out in adolescents with epilepsy and only a few studies have compared color perception in epileptic patients receiving different AEDs or monotherapy.[1–11]

The aims of our study were to evaluate whether deficit exists in color vision in epileptic children and adolescents, to study if the treatment with AEDs monotherapy can affect color vision measured with three different tests and to determine the possible relationship between abnormal color vision tests and AEDs dosage and their serum concentrations.

Patients

We studied 45 epileptic adolescents (16 males and 29 females, mean age 15.71 ± 2.01 years: range 11–18), suffering from various types of epilepsy. Patients were recruited from the Departments of Pediatrics and Ophthalmology, University of Chieti in Italy, and they were newly diagnosed and treatment free prior to the study.

Patients with familiar and/or personal history of congenital color disturbances with the Ishihara color test, a history of ocular trauma or pathology or poor vision were excluded.

Patients included in this study were examined before and after 1 year of therapy with different AEDs monotherapy. None of the studied patients complained of color vision disturbances.

After the baseline evaluation, the patients were subdivided into two groups according to their therapy: 29 patients (19 females, 10 males; mean age 13.5 ± 1.8 years) treated with CBZ and 16 patients (10 females, 6 males; mean age 16.4 ± 2.1 years) treated with VPA. The AED used was chosen according to the type of epilepsy of the patients; CBZ was the drug used particularly in partial epilepsies, whereas VPA was primarily used in primary generalized epilepsies. Gender and sex ratio were similar in the two groups. In the two groups of patients, the AEDs were prescribed at the normal dosage and all serum levels of AEDs were within the therapeutic range during the time of the study.

Forty healthy sex- and age-matched children served as controls which were not treated with any AEDs and fulfilled all inclusion criteria.

Informed consent was obtained by the parents and assent by the adolescents; consent was obtained also in the control groups. The study was approved by the Ethical Committee of the University of Chieti.

Before the beginning of the study, detailed ophthalmological evaluation was performed by one of the authors (L.L.) on each patient and control, which included: visual acuity, slit-lamp biomicroscopy, intraocular pressure measurement, direct and indirect ophthalmoscopy, fundus retinography. All these examinations were normal.

All patients and controls underwent the following monocular examinations before the beginning of therapy, testing the right eye first: (1) chromatic sense (FM100 hue test) with the evaluation of total error score (TES); (2) two white-on-white threshold visual fields, performed at least 2 days before the test visual field, to reduce learning effect, not evaluated in the study; and (3) central static automated perimetry (pupil size greater than 3 mm), performed with both white-on-white and blue-on-yellow stimuli (short-wavelength automated perimetry—SWAP).

The previously described ophthalmological evaluation was performed again at the end of the follow-up.

VPA and CBZ serum concentrations were determined on the same day of the second ophthalmological evaluation, by a capillary gas chromatography method.

Methods

The FM100 hue test

This test consists of colored caps as previously described.[12,13] In detail, there are four boxes in this test; the first includes the hues from red to yellowish green, the second from yellowish green to bluish green, the third from bluish green to violet, and the fourth from violet to red. The testee has to arrange the caps according to the hues from the first to the last fixed hue of the box. The order of presentation of the boxes was varied randomly between patients. No time limit was prescribed and the subjects were allowed to correct each of his arrangements. Each patient performed the test under standard lighting conditions using natural daylight in sunny days. In presence of cloudy days the test was postponed. Each eye was tested separately with correction of refractive defects. After completion of the test TES values were calculated for each patient using the Farnsworth method. The main axis of color confusion was determined for each test.

Achromatic and short-wavelength automated perimetry

Static perimetry was performed using the full-threshold 24-2 program of a modified Humphrey Field Analyser 640 (Humphrey Instruments, San Leandro, CA, USA).

The test was performed in both eyes. Foveal threshold and mean threshold perimetric sensitivity for each group, for each area and for each test (achromatic perimetry and SWAP) were evaluated. A subdivision of the visual field in three concentric areas was performed as previously described.[14] Area 1 extends from the center up to 9°, area 2 from 9 up to 18°, and area 3 from 18 up to 24/30°.

Both for achromatic perimetry and SWAP we used parameters and technique as previously described.[15]

For achromatic perimetry, the parameters used were background luminance, 31.5 apostilb; stimulus size, Goldmann III; and stimulus color, white. The background illumination was extinguished using standard Humphrey software. A bright yellow background of 80.9 cd/m^2, producing a retinal illuminance of ~2.8 photopic trolands was produced using a carousel projector mounted on the left side of the perimeter cabinet as suggested by Sample and Weinreb.[16] Wratten #12 filters were placed in front of all background sources to produce a yellow background. Then, we adjusted and calibrated the background until it displayed equal luminance across the central 30° of the visual field. A filter holder was placed in the stimulus light path just behind the perimeter's shutter box, and a 440-nm interference filter (half-band-width of 4 nm) was inserted into the holder.[16] The modification for SWAP became operative after the instrument had performed its standard internal calibration routine.

Statistical analysis

All data are presented as the means ± S.D. For statistical analysis only the right eye was evaluated. The statistical analysis was performed with the SPSS/PC program (Release 6.0, 444. Chicago, IL, USA). To evaluate intergroup differences we used ANOVA with Scheffe's post hoc test, when appropriate. Repeated measures ANOVA was used to evaluate the intragroup modifications of TES and perimetric threshold during the follow-up.

To determine if there was a significant correlation between chromatic sense and perimetric data and AEDs dosage and serum concentrations, Pearson's correlation test was performed.

P values <0.05 were considered statistically significant.

Results

The FM100 hue test

At the beginning of the study, all epileptic adolescents showed TES values similar to control values (Table 1).

Table 1 Central color vision tested with FM100 hue test in CBZ and VPA epileptic patients and in control subjects.

	Cases (n)	Baseline (TES)	After therapy or no therapy (TES)	Percentage change from baseline
CBZ patients	29	110.65 ± 22.9	166.00 ± 27.72*	+50.02
VPA patients	16	107.43 ± 21.70	151.19 ± 44.09*	+40.73
Controls	40	109.11 ± 22.1	109.29 ± 24.73	+0.16

Data are means ± S.D. TES: total error score.
* $P < 0.001$ vs. baseline and controls.

At the end of the follow-up a significant ($P < 0.001$) higher number of errors was found in both groups of patients in comparison with controls and baseline values (Table 1). In particular, TES values were above the normal age-dependent ranges in 14 CBZ patients (48.28%) and in 7 VPA patients (43.75%). In all these patients the greatest number of errors was in the third (green-blue) box of the FM100 hue test. In 11 CBZ patients (37.93%) and in 6 VPA patients (37.50%) the main axis of color confusion was in blue-yellow area. In other cases it was not possible to determine a preferential confusion axis.

Achromatic perimetry

Mean test time was 13.45 min (±3.76) for patients and 13.17 min (±3.47) for controls. In all cases of both groups, the false positives, negatives, and fixation losses were below 15%. At the beginning of the study both foveal threshold and full-field and subareas mean sensitivities were similar in the two groups of patients and in controls (Tables 2 and 3).

At the end of the follow-up, patients of both groups showed no significant change of mean test time, foveal threshold, mean full-field threshold perimetric sensitivity, and mean threshold perimetric sensitivity of the three evaluated subareas (Tables 4–6).

SWAP

Mean test time was 16.32 min (±4.12) for patients and 16.27 min (±3.91) for controls. In all cases of both groups, the false positives, negatives, and fixation losses were below 15%.

Foveal threshold and full-field mean threshold perimetric sensitivity of both groups of patients, at the beginning and at the end of the follow-up is shown in Tables 2 and 3.

The subdivision of the visual fields in three concentric areas showed similar results in the three

Table 2 Foveal threshold tested with achromatic and color perimetry in CBZ and VPA epileptic patients and in control subjects.

	Cases (*n*)	Baseline (dB)	After therapy or no therapy (dB)	Percentage change from baseline
Achromatic perimetry				
CBZ patients	29	33.55 ± 1.45	33.01 ± 1.41	−1.61
VPA patients	16	33.19 ± 1.11	33.31 ± 1.54	+0.36
Controls	40	33.16 ± 1.09	33.24 ± 1.08	+0.24
Color perimetry				
CBZ patients	29	21.66 ± 1.90	19.35 ± 1.32*	−10.67
VPA patients	16	22.06 ± 2.75	18.88 ± *1.89**	−14.42
Controls	40	21.03 ± 2.25	21.07 ± *2.01*	+0.19

Data are means ± S.D. dB: decibel.
*$P < 0.001$ vs. baseline and controls.

Table 3 Full-field mean perimetric sensitivity tested with achromatic and color perimetry in CBZ and VPA epileptic patients and in control subjects.

	Cases (*n*)	Baseline (dB)	After therapy or no therapy (dB)	Percentage change from baseline
Achromatic perimetry				
CBZ patients	29	29.82 ± 0.93	29.72 ± 0.99	−0.33
VPA patients	16	29.67 ± 0.81	30.02 ± 0.97	+1.17
Controls	40	29.50 ± 0.60	29.74 ± 0.50	+0.81
Color perimetry				
CBZ patients	29	18.90 ± 1.35	16.60 ± 1.47*	−12.17
VPA patients	16	18.73 ± 1.35	16.23 ± 1.55*	−13.35
Controls	40	18.60 ± 1.25	18.50 ± 1.24	−0.54

Data are means ± S.D. dB: decibel.
*$P < 0.001$ vs. baseline and controls.

Table 4 Mean perimetric sensitivity in area 1 (0—9°) of the visual field tested with achromatic and color perimetry in CBZ and VPA epileptic patients and in control subjects.

	Cases (*n*)	Baseline (dB)	After therapy or no therapy (dB)	Percentage change from baseline
Achromatic perimetry				
CBZ patients	29	31.48 ± 1.92	31.17 ± 1.61	−0.98
VPA patients	16	31.13 ± 1.99	31.56 ± 1.87	+1.38
Controls	40	31.30 ± 1.55	31.25 ± 1.45	−0.15
SWAP				
CBZ patients	29	21.10 ± 1.35	19.45 ± 1.74*	−7.81
VPA patients	16	21.00 ± 1.27	18.25 ± 1.61*	−13.10
Controls	40	21.00 ± 1.25	21.01 ± 1.15	+0.05

Data are means ± S.D. dB: decibel.
*$P = 0.001$ vs. baseline and controls.

Table 5 Mean perimetric sensitivity in area 2 (10—18°) of the visual field tested with achromatic and color perimetry in CBZ and VPA epileptic patients and in control subjects.

	Cases (*n*)	Baseline (dB)	After therapy or no therapy (dB)	Percentage change from baseline
Achromatic perimetry				
CBZ patients	29	29.48 ± 1.15	28.48 ± 1.18	−3.39
VPA patients	16	29.25 ± 0.68	29.50 ± 0.89	+0.85
Controls	40	29.35 ± 1.01	29.45 ± 1.21	+0.34
Color perimetry				
CBZ patients	29	18.59 ± 1.50	16.07 ± 1.58*	−13.56
VPA patients	16	18.00 ± 1.93	16.13 ± 1.46*	−10.39
Controls	40	18.60 ± 1.53	18.40 ± 1.43	−1.08

Data are means ± S.D. dB: decibel.
*$P < 0.001$ vs. baseline and controls.

Table 6 Mean perimetric sensitivity in area 3 (>18°) of the visual field tested with achromatic and color perimetry in CBZ and VPA epileptic patients and in control subjects.

	Cases (*n*)	Baseline (dB)	After therapy or no therapy (dB)	Percentage change from baseline
Achromatic perimetry				
CBZ patients	29	28.79 ± 1.42	28.48 ± 1.18	−1.08
VPA patients	16	28.63 ± 1.15	29.00 ± 0.97	+1.29
Controls	40	28.50 ± 1.35	28.45 ± 1.25	−0.18
Color perimetry				
CBZ patients	29	17.07 ± 1.41	14.28 ± 1.51*	−16.35
VPA patients	16	17.19 ± 1.38	14.31 ± 2.90*	−16.75
Controls	40	17.10 ± 1.39	17.20 ± 1.49	−0.59

Data are means ± S.D. dB: decibel.
*$P < 0.001$ vs. baseline and controls.

subareas. At the end of follow-up, in both groups of patients in all evaluated subareas a significant decrease of threshold perimetric sensitivity was found (Tables 4–6).

Finally, no significant correlation was found between daily dosage and serum levels of AEDs and the results of the color vision tests.

Discussion

The present study suggests that epileptic patients do not have color vision dysfunction but they show significant disturbances after 1 year of treatment with VPA and CBZ monotherapy.

In recent years, many authors have suggested that adult epileptic patients treated with these AEDs can have this side effect.[2–7,13] We have studied the effect of CBZ and VPA on visual perception using three different methods. In particular, we have evaluated color vision both in the fixation point using the FM100 hue test and for the first time, in the paracentral area using perimetry in the blue-yellow axis. Moreover, achromatic perimetry was performed in all patients.

The FM100 hue test is the most sensitive test for detection of color discrimination deficit but it evaluates only foveal color vision. This technique has been widely used in other studies because it is a commonly available reference for the description of a color perception deficit.[17] Mild subclinical impairment of color perception is often one of the earliest signs of visual dysfunction.[1] It is interesting to underline that we found an impressive consistency of the TES values for the control group before and after treatment: this fact suggests an excellent reproducibility of the technique.

Particularly, in many ocular affections (e.g. macular disease, diabetes, glaucoma), it has been demonstrated that color vision impairment is an early sign of disease. Furthermore, many papers have underlined the role of SWAP in the early diagnosis of many other diseases.[15,16,18,19] Recent studies carried out SWAP visual field testing on VGB-treated epilepsy patients.[20,21] Daneshvar et al.[20] identified SWAP defects outside 10°, while Roff Hilton et al. found defects within the central 10° field. In our study we identified defects dispersed both within the central 10° field and in outside the of 10° field.

It is well known that color vision is a sensitive indicator of altered perception or transmission of the neurosensorial signal: it relies on a very subtle balance of the outputs of the three different cone photoreceptors on postreceptoral retinal neurons. Moreover, achromatic perimetry is not useful in the detection of the vision abnormalities caused by these AEDs while significant abnormalities have been found in both groups of patients using the SWAP. For the first time we have compared achromatic and SWAP for the evaluation of this side effect of AEDs: from our experience, SWAP seems to be very useful in determining that color deficit is located in foveal area and in parafoveal area (0–9°) and also up to 30°.

According to other studies,[4,13,22] our findings suggest that the effect of CBZ and VPA on calcium and sodium membrane conductances may play a role in color vision deficits induced by these AEDs. CBZ and VPA operate by blocking voltage-dependent sodium channels, but it has been suggested that VPA also down-regulates the function of the T-type calcium channel and/or GABA receptor channel. It is likely that AEDs have a negative effect on the retinal cell layer by changes induced upon glutamate and other neurotransmitters. It has not yet been demonstrated whether this negative effect is more pronounced on photoreceptors and/or on on-off receptors of bipolar cells. The selective loss of short-wavelength-sensitive cone signals (blue), found in our and other studies,[2] can be explained by anatomical and physiological differences between the blue-yellow and red-green systems.[23] In fact, it is well known that both visual acuity and contrast sensitivity are poorer in blue light than in red or green light.[24,25] This phenomenon may be due in part to the relative paucity of the short-wavelength-sensitive cones compared to medium and long-wavelength-sensitive cones. Moreover, blue light is color contrasted with yellow light and is encoded in the color opponent and double opponent cells that signal simultaneous contrast of blue and yellow in adjacent locations. The possibility to evaluate specifically central visual field, avoiding to stimulate all sensitive cones using white stimuli, allows an earlier diagnosis of color visual impairment in several ocular diseases, such as diabetes and glaucoma.[12,14–16]

We did not find a significant correlation between daily dosage and/or serum levels of AED and the results of vision tests. This lack of correlation, reported also by other authors[2,4,7] can be explained by the several mechanisms involved in the vision function that probably is not directly affected only by AEDs.

Furthermore, computerized perimetry, being a fully computer-controlled system, avoids errors due to the human intervention or interpretation; it allows sensitive statistical analysis very useful in the early diagnosis and long-term follow-up of several ocular affections.

It is well known that the trichromatic properties of human color vision are easily demonstrable out to between 20 and 30° way from fixation: this fact can explain the usefulness of SWAP.

In conclusion, although the visual deficits are not severe enough to produce subjective visual complaints, our study confirms that epileptic patients treated with VPA and CBZ can show color vision defects, in particular for blue vision and that these defects are well evidenced by the FM100 hue test. These abnormalities are present not only in the foveal area but also in the peripheral areas. Moreover, while achromatic perimetry seems to be an insensitive technique to these changes, SWAP is more sensitive capable detecting early color dysfunction not only in central but also in peripheral areas. Consequently, we advise clinicians to carry out this evaluation in epileptic patients who are treated with VPA and/or CBZ. At this stage, the study cannot clarify if the effects on color vision are transient or chronic and if they are reversible.

References

1. Mecarelli O, Rinalduzzi S, Accornero N. Changes in color vision after a single dose of vigabatrin or carbamazepine in healthy volunteers. *Clin Neuropharmacol* 2001;**24**:23—6.
2. Bayer AU, Thiel HJ, Zrenner E, Dichgans J, Kuehn M, Paulus W, et al. Color vision tests for early detection of antiepileptic drug toxicity. *Neurology* 1997;**48**:1394—7.
3. Nousiainen I, Kalvainen R, Mantyjarvi M. Color vision in epilepsy patients treated with vigabatrin or carbamazepine monotherapy. *Ophathalmology* 2000;**107**:884—8.
4. Lopez L, Thomson A, Rabinowicz AL. Assessment of colour vision in epileptic patients exposed to single-drug therapy. *Eur Neurol* 1999;**41**:201—5.
5. Steinhoff BJ, Freudenthaler N, Paulus W. The influence of established and new antiepilectic drugs on visual perception. I. A placebo-controlled, double-blind, single-dose study in healthy volunteers. *Epilepsy Res* 1997;**29**:35—47.
6. Steinhoff BJ, Freudenthaler N, Paulus W. The influence of established and new antiepilectic drugs on visual perception. II. A controlled study in patients with epilepsy under long-term antiepilectic medication. *Epilepsy Res* 1997;**29**:49—58.
7. Nousiainen I, Kalvainen R, Mantyjarvi M. Contrast and glare sensitivity in epilepsy patients treated with vigabatrin or carbamazepine monotherapy compared with healthy volunteers. *Br J Ophthalmol* 2000;**84**:622—5.
8. Tomson T, Nilsson BY, Levi R. Impaired visual contrast sensitivity in epileptic patients treated with carbamazepine. *Arch Neurol* 1988;**45**:897—900.
9. Bayer A. *Retinale funktionsstorungen bej patienten unter antikonvulsiver therapje*. Medical Thesis, University of Tubingen, 1991.
10. Stamper RL. The effect of glaucoma on central visual function. *Trans Am Ophthalmol Soc* 1984;**82**:792—826.
11. Accornero N, Gregori B, Galiè E, De Feo A, Agnesi R. A new color VEP procedure discloses asymptomatic visual impairments in optic neuritis and glaucoma suspects. *Acta Neurol Scand* 2000;**102**:258—63.
12. Verrotti A, Lobefalo L, Chiarelli F, Mastropasqua L, Ciancaglini M, Morgese G. Color vision and persistent microalbuminuria in children with type-1 (insulin-dependent) diabetes mellitus: a longitudinal study. *Diabetes Res Clin Pract* 1995;**30**:125—30.
13. Paulus W, Schwarz G, Steinhoff BJ. The effect of anti-epilectic drugs on visual perception in patients with epilepsy. *Brain* 1996;**119**:539—49.
14. Mastropasqua L, Verrotti A, Lobefalo L, Chiarelli F, Verdesea G, Morgese G. Visual field defects in diabetic children without retinopathy: relation between visual function and microalbuminuria. *Acta Ophthalmol Scand* 1995;**73**:125—8.
15. Lobefalo L, Verrotti A, Mastropasqua L, Della Loggia G, Cherubini V, Morgese G, et al. Blue-on-yellow and achromatic perimetry in diabetic children without retinopathy. *Diabetes Care* 1998;**21**:2003—6.
16. Sample PA, Weinreb RN. Color perimetry for assessment of primary open-angle glaucoma. *Invest Ophthalmol Vis Sci* 1990;**31**:1869—75.
17. Pokorny J, Smith VC, Verriest G, Pinckers AJLG. *Congenital and acquired color vision defects*. New York: Grune Stratton; 1979.
18. Accornero N, Capozza M, De Feo A, Rinalduzzi S, De Marinis M, Pecori-Giraldi J, et al. Video color perimetry: impairment in glaucoma suspects. *Doc Ophthalmol* 2001;**103**:81—90.
19. Harwerth RS, Smith III EL, Chandler M. Progressive visual field defects from experimental glaucoma: measurements with white and colored stimuli. *Optom Vis Sci* 1999;**76(8)**:558—70.
20. Daneshvar H, Racette L, Coupland SG, Kertes PJ, Guberman A, Zackon D. Symptomatic and asymptomatic visual loss in patients taking vigabatrin. *Ophthalmology* 1999;**106**:1792—8.
21. Hilton EJ, Cubbidge RP, Hosking SL, Betts T, Comaish IF. Patients treated with vigabatrin exhibit central visual function loss. *Epilepsia* 2002;**43**:1351—9.
22. MacDonald RL, Kelly KM. Mechanisms of action of currently prescribed and newly developed antiepilectic drugs [review]. *Epilepsia* 1994;**35(Suppl 4)**:S41—50.
23. Ahnelt PK, Kolb H. Short-wavelength-sensitive cones: morphology and color-specific connections. In: Drum B, editor. *Colour vision deficiencies XII*. Dordrecht: Kluwer; 1995. p. 285–97.
24. Brindley GS. The summation areas of human colour receptive mechanisms at increment threshold. *J Physiol (Lond)* 1954;**124**:400.
25. Green DG. The contrast sensitivity of the colour mechanisms of the human eye. *J Physiol (Lond)* 1968;**196**:415.